

## EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	332	DMXAA	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2006/11/08 09:35
L2	4279	gemcitabine	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	OR	OFF	2006/11/08 09:35
L3	67	L1 L2	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	OFF	2006/11/08 09:47
L4	45498	wilson.in.	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	OFF	2006/11/08 09:36
L5	7	L1 L4	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	AND	OFF	2006/11/08 09:36
L6	2	l1 l2	US-PGPUB; USPAT; USOCR; FPRS; EPO; JPO; DERWENT	NEAR	OFF	2006/11/08 09:47

10/790,943

- SEARCH HISTORY

FILE 'HOME' ENTERED AT 09:12:12 ON 08 NOV 2006

=> file medline, caplus, wpids, uspatfull

=> s "DMXAA" or "5,6-dimethyl-xanthenone-4 acetic acid"

L1 538 "DMXAA" OR "5,6-DIMETHYL-XANTHENONE-4 ACETIC ACID"

=> s "gemcitabine"

L2 11744 "GEMCITABINE"

=> s "vascular targeting agent?"

L3 229 "VASCULAR TARGETING AGENT?"

=> s "solid tumor?"

L4 16897 "SOLID TUMOR?"

=> s l1 and l2

L5 71 L1 AND L2

=> s l2 and l3

L6 43 L2 AND L3

=> s l5 and l4

L7 38 L5 AND L4

=> s l1 and l2 and l3

L8 23 L1 AND L2 AND L3

=> s l8 and l4

L9 19 L8 AND L4

=> s l5 not py>2001

L10 0 L5 NOT PY>2001

=> s l6 not py>2001

L11 0 L6 NOT PY>2001

=> s l7 not py>2001

L12 0 L7 NOT PY>2001

=> s l5 not py>2002

L13 1 L5 NOT PY>2002

=> d l13 ibib, abs

L13 ANSWER 1 OF 1 USPATFULL on STN

ACCESSION NUMBER: 2002:213736 USPATFULL Full-text

TITLE: Neutrokin-alpha and Neutrokin-alpha splice variant

INVENTOR(S): Yu, Guo-Liang, Berkeley, CA, UNITED STATES

Ebner, Reinhard, Gaithersburg, MD, UNITED STATES

Ni, Jian, Germantown, MD, UNITED STATES

Rosen, Craig A., Laytonsville, MD, UNITED STATES

Ullrich, Stephen, Rockville, MD, UNITED STATES

PATENT ASSIGNEE(S): Human Genome Sciences, Inc., Rockville, MD, UNITED STATES, 20850 (U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 2002115112 A1 20020822

APPLICATION INFO.: US 2001-929493 A1 20010815 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2000-588947, filed on 8 Jun 2000, PENDING Continuation-in-part of Ser. No. US 2000-589285, filed on 8 Jun 2000, PENDING Continuation-in-part of Ser. No. US 2000-589286, filed on 8 Jun 2000, PENDING Continuation-in-part of Ser. No. US 2000-589287, filed on 8 Jun 2000, PENDING Continuation-in-part of Ser. No. US 2000-586288, filed on 2 Jun 2000, PATENTED Continuation-in-part of Ser. No. US 2000-507968, filed on 22 Feb 2000, PENDING Continuation-in-part of Ser. No. US 1999-255794, filed on 23 Feb 1999, PENDING Continuation-in-part of Ser. No. US 1999-255794, filed on 23 Feb 1999, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-225628P	20000815 (60)
	US 2000-227008P	20000823 (60)
	US 2000-234338P	20000922 (60)
	US 2000-240806P	20001017 (60)
	US 2000-250020P	20001130 (60)
	US 2001-276248P	20010316 (60)
	US 2001-293499P	20010525 (60)
	US 2001-296122P	20010607 (60)
	US 2001-304809P	20010713 (60)
	US 1999-122388P	19990302 (60)
	US 1999-124097P	19990312 (60)
	US 1999-126599P	19990326 (60)
	US 1999-127598P	19990402 (60)
	US 1999-130412P	19990416 (60)
	US 1999-130696P	19990423 (60)
	US 1999-131278P	19990427 (60)
	US 1999-131673P	19990429 (60)
	US 1999-136784P	19990528 (60)
	US 1999-142659P	19990706 (60)
	US 1999-145824P	19990727 (60)
	US 1999-167239P	19991124 (60)
	US 1999-168624P	19991203 (60)
	US 1999-171108P	19991216 (60)
	US 1999-171626P	19991223 (60)
	US 2000-176015P	20000114 (60)

DOCUMENT TYPE: Utility  
FILE SEGMENT: APPLICATION  
LEGAL REPRESENTATIVE: HUMAN GENOME SCIENCES INC, 9410 KEY WEST AVENUE, ROCKVILLE, MD, 20850  
NUMBER OF CLAIMS: 117  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 22 Drawing Page(s)  
LINE COUNT: 18178

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to nucleic acid molecules encoding Neutrokin-  
alpha and/or Neutrokin-alphaSV polypeptides, including soluble forms of the  
extracellular domain. Neutrokin-alpha and/or Neutrokin-alphaSV  
polypeptides are also provided as are vectors, host cells and recombinant  
methods for producing the same. The invention further relates to antibodies  
or portions thereof that specifically bind Neutrokin-alpha and/or  
Neutrokin-alphaSV and diagnostic and therapeutic methods using these  
antibodies. Also provided are diagnostic methods for detecting immune  
system-related disorders and therapeutic methods for treating immune system-  
related disorders using the compositions of the invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 19 1-19 ibib, abs

L9 ANSWER 1 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2006:267618 USPATFULL Full-text  
TITLE: Constructs binding to phosphatidylserine and their use  
in disease treatment  
INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES  
Luster, Troy A., Dallas, TX, UNITED STATES  
King, Steven W., Ladera Ranch, CA, UNITED STATES  
PATENT ASSIGNEE(S): Board of Regents, The University of Texas System (U.S.  
corporation)  
Peregrine Pharmaceuticals, Inc. (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2006228299	A1	20061012
APPLICATION INFO.:	US 2006-339392	A1	20060124 (11)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2005-646333P	20050124 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	PEREGRINE PHARMACEUTICALS, INC., 5353 WEST ALABAMA, SUITE 306, HOUSTON, TX, 77056, US	
NUMBER OF CLAIMS:	35	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	28 Drawing Page(s)	
LINE COUNT:	12525	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are new phosphatidylserine binding constructs with surprising combinations of properties, and a range of diagnostic and therapeutic conjugates thereof. The new constructs effectively bind phosphatidylserine targets in disease and enhance their destruction, and can also specifically deliver attached imaging or therapeutic agents to the disease site. Also disclosed are methods of using the new construct compositions, therapeutic conjugates and combinations thereof in tumor vasculature targeting, cancer diagnosis and treatment, and for treating viral infections and other diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 2 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2005:157851 USPATFULL Full-text  
TITLE: Cancer treatment methods using selected antibodies to  
aminophospholipids  
INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES  
Ran, Sophia, Riverton, IL, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005136059	A1	20050623
APPLICATION INFO.:	US 2003-642071	A1	20030815 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2003-621269, filed on 15 Jul 2003, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-396263P	20020715 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	WILLIAMS, MORGAN & AMERSON, P.C., 10333 RICHMOND, SUITE 1100, HOUSTON, TX, 77042, US	
NUMBER OF CLAIMS:	20	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	53 Drawing Page(s)	
LINE COUNT:	13044	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 3 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2005:150785 USPATFULL Full-text  
 TITLE: Cancer treatment methods using selected  
 immunoconjugates for binding to aminophospholipids  
 INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES  
 Ran, Sophia, Riverton, IL, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005129696	A1	20050616
APPLICATION INFO.:	US 2003-642065	A1	20030815 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2003-621269, filed on 15 Jul 2003, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-396263P	20020715 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	WILLIAMS, MORGAN & AMERSON, P.C., 10333 RICHMOND, SUITE 1100, HOUSTON, TX, 77042, US	
NUMBER OF CLAIMS:	23	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	53 Drawing Page(s)	
LINE COUNT:	13046	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 4 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2005:69437 USPATFULL Full-text  
TITLE: Compositions comprising phosphatidylethanolamine-  
binding peptides linked to anti-viral agents  
INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES  
Soares, M. Melina, Richardson, TX, UNITED STATES  
He, Jin, Dallas, TX, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005059578	A1	20050317
APPLICATION INFO.:	US 2003-642121	A1	20030815 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2003-621269, filed on 15 Jul 2003, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-396263P	20020715 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	WILLIAMS, MORGAN & AMERSON, P.C., 10333 RICHMOND, SUITE 1100, HOUSTON, TX, 77042	
NUMBER OF CLAIMS:	21	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	53 Drawing Page(s)	
LINE COUNT:	13308	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 5 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2005:36945 USPATFULL Full-text  
TITLE: Combined cancer treatment methods using selected  
antibodies to aminophospholipids  
INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES  
Huang, Xianming, Dallas, TX, UNITED STATES  
Ran, Sophia, Riverton, IL, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005031620	A1	20050210
APPLICATION INFO.:	US 2003-642058	A1	20030815 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2003-621269, filed on 15 Jul 2003, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-396263P	20020715 (60)

DOCUMENT TYPE: Utility  
 FILE SEGMENT: APPLICATION  
 LEGAL REPRESENTATIVE: WILLIAMS, MORGAN & AMERSON, P.C., 10333 RICHMOND, SUITE  
 1100, HOUSTON, TX, 77042  
 NUMBER OF CLAIMS: 33  
 EXEMPLARY CLAIM: 1  
 NUMBER OF DRAWINGS: 53 Drawing Page(s)  
 LINE COUNT: 13439  
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 6 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2005:30331 USPATFULL Full-text  
 TITLE: Anti-viral treatment methods using  
 phosphatidylethanolamine-binding peptides linked to  
 anti-viral agents  
 INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES  
 Soares, M. Melina, Richardson, TX, UNITED STATES  
 He, Jin, Dallas, TX, UNITED STATES  
 PATENT ASSIGNEE(S): Board of Regents, The University of Texas System (U.S.  
 corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005025761	A1	20050203
APPLICATION INFO.:	US 2003-642100	A1	20030815 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2003-621269, filed on 15 Jul 2003, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-396263P	20020715 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	WILLIAMS, MORGAN & AMERSON, P.C., 10333 RICHMOND, SUITE 1100, HOUSTON, TX, 77042	
NUMBER OF CLAIMS:	23	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	52 Drawing Page(s)	
LINE COUNT:	13426	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		

AB Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 7 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2005:3839 USPATFULL Full-text  
TITLE: Combinations and kits for cancer treatment using  
selected antibodies to aminophospholipids  
INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES  
Huang, Xianming, Dallas, TX, UNITED STATES  
Ran, Sophia, Riverton, IL, UNITED STATES  
PATENT ASSIGNEE(S): Board of Regents, The University of Texas System (U.S.  
corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005002941	A1	20050106
APPLICATION INFO.:	US 2003-642116	A1	20030815 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2003-621269, filed on 15 Jul 2003, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-396263P	20020715 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	WILLIAMS, MORGAN & AMERSON, P.C., 10333 RICHMOND, SUITE 1100, HOUSTON, TX, 77042	
NUMBER OF CLAIMS:	28	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	53 Drawing Page(s)	
LINE COUNT:	13468	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 8 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2004:334289 USPATFULL Full-text  
TITLE: Liposomes coated with selected antibodies that bind to  
aminophospholipids  
INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES  
Huang, Xianming, Dallas, TX, UNITED STATES  
Ran, Sophia, Riverton, IL, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004265367	A1	20041230
APPLICATION INFO.:	US 2003-642064	A1	20030815 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2003-621269, filed on 15 Jul 2003, PENDING		

NUMBER	DATE
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PRIORITY INFORMATION: US 2002-396263P 20020715 (60)  
DOCUMENT TYPE: Utility  
FILE SEGMENT: APPLICATION  
LEGAL REPRESENTATIVE: WILLIAMS, MORGAN & AMERSON, P.C., 10333 RICHMOND, SUITE  
1100, HOUSTON, TX, 77042  
NUMBER OF CLAIMS: 23  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 53 Drawing Page(s)  
LINE COUNT: 13511  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycinbased compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 9 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2004:279855 USPATFULL Full-text  
TITLE: Selected immunoconjugates for binding to  
aminophospholipids  
INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES  
Ran, Sophia, Riverton, IL, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004219155	A1	20041104
APPLICATION INFO.:	US 2003-642099	A1	20030815 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2003-621269, filed on 15 Jul 2003, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-396263P	20020715 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Shelley P.M. Fussey, Williams, Morgan & Amerson, P.C., Suite 1100, 10333 Richmond, Houston, TX, 77042	
NUMBER OF CLAIMS:	31	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	53 Drawing Page(s)	
LINE COUNT:	13474	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 10 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2004:274262 USPATFULL Full-text  
TITLE: Anti-viral treatment methods using  
phosphatidylethanolamine-binding peptide derivatives  
INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES  
Soares, M. Melina, Richardson, TX, UNITED STATES  
He, Jin, Dallas, TX, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004214764	A1	20041028
APPLICATION INFO.:	US 2003-642117	A1	20030815 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2003-621269, filed on 15 Jul 2003, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-396263P	20020715 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Shelley P.M. Fussey, WILLIAMS, MORGAN & AMERSON, P.C., Suite 1100, 10333 Richmond, Houston, TX, 77042	
NUMBER OF CLAIMS:	25	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	53 Drawing Page(s)	
LINE COUNT:	13426	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 11 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2004:273287 USPATFULL Full-text  
TITLE: Methods for treating viral infections using  
immunoconjugates to aminophospholipids  
INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES  
Soares, M. Melina, Richardson, TX, UNITED STATES  
Ran, Sophia, Riverton, IL, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004213779	A1	20041028
APPLICATION INFO.:	US 2003-642119	A1	20030815 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2003-621269, filed on 15 Jul 2003, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-396263P	20020715 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	

LEGAL REPRESENTATIVE: Shelley P.M. Fussey, Williams, Morgan & Amerson, P.C.,  
Suite 1100, 10333 Richmond, Houston, TX, 77042

NUMBER OF CLAIMS: 31

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 53 Drawing Page(s)

LINE COUNT: 13438

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 12 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2004:267331 USPATFULL Full-text

TITLE: Selected antibody CDRs for binding to  
aminophospholipids

INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES

Ran, Sophia, Riverton, IL, UNITED STATES

PATENT ASSIGNEE(S): Board of Regents, The University of Texas System (U.S.  
corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004208868	A1	20041021
APPLICATION INFO.:	US 2003-642118	A1	20030815 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2003-621269, filed on 15 Jul 2003, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-396263P	20020715 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Shelley P.M. Fussey, Williams,, Morgan & Amerson, P.C., 10333 Richmond, Suite 1100, Houston, TX, 77042	
NUMBER OF CLAIMS:	19	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	53 Drawing Page(s)	
LINE COUNT:	13435	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 13 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2004:226993 USPATFULL Full-text  
TITLE: Selected antibody compositions and methods for binding  
to aminophospholipids  
INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES  
Ran, Sophia, Riverton, IL, UNITED STATES  
PATENT ASSIGNEE(S): Board of Regents, The University of Texas System (U.S.  
corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004175378	A1	20040909
APPLICATION INFO.:	US 2003-620850	A1	20030715 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-396263P	20020715 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Shelley P.M. Fussey, Williams, Morgan & Amerson, P.C., Suite 1100, 10333 Richmond, Houston, TX, 77042	
NUMBER OF CLAIMS:	19	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	53 Drawing Page(s)	
LINE COUNT:	12773	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 14 OF 19 USPATFULL on STN  
ACCESSION NUMBER: 2004:220853 USPATFULL Full-text  
TITLE: Selected antibody compositions for binding to  
aminophospholipids  
INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES  
Ran, Sophia, Riverton, IL, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004170620	A1	20040902
APPLICATION INFO.:	US 2003-621269	A1	20030715 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-396263P	20020715 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Shelley P.M. Fussey, Williams, Morgan & Amerson, P.C., Suite 1100, 10333 Richmond, Houston, TX, 77042	
NUMBER OF CLAIMS:	92	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	53 Drawing Page(s)	
LINE COUNT:	13072	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 15 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2004:208997 USPATFULL Full-text

TITLE: Compositions for treating viral infections using immunoconjugates to aminophospholipids

INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES  
Soares, M. Melina, Richardson, TX, UNITED STATES  
Ran, Sophia, Riverton, IL, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004161429	A1	20040819
APPLICATION INFO.:	US 2003-642124	A1	20030815 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2003-621269, filed on 15 Jul 2003, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-396263P	20020715 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	WILLIAMS, MORGAN & AMERSON, P.C., 10333 RICHMOND, SUITE 1100, HOUSTON, TX, 77042	
NUMBER OF CLAIMS:	22	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	53 Drawing Page(s)	
LINE COUNT:	13334	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycinbased compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 16 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2004:190667 USPATFULL Full-text

TITLE: Compositions comprising cell-impermeant duramycin derivatives

INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES  
He, Jin, Dallas, TX, UNITED STATES

PATENT ASSIGNEE(S): Board of Regents, The University of Texas System (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004147440	A1	20040729
APPLICATION INFO.:	US 2003-642059	A1	20030815 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2003-621269, filed on 15 Jul 2003, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-396263P	20020715 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Shelley P.M. Fussey, WILLIAMS, MORGAN & AMERSON, P.C., Suite 1100, 10333 Richmond, Houston, TX, 77042	
NUMBER OF CLAIMS:	16	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	53 Drawing Page(s)	
LINE COUNT:	13402	
CAS INDEXING IS AVAILABLE FOR THIS PATENT.		

AB Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 17 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2004:171463 USPATFULL Full-text

TITLE: Combinations and kits for treating viral infections using immunoconjugates to aminophospholipids

INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES  
Soares, M. Melina, Richardson, TX, UNITED STATES  
Ran, Sophia, Riverton, IL, UNITED STATES

PATENT ASSIGNEE(S): Board of Regents (U.S. corporation)  
The University of Texas System (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004131622	A1	20040708
APPLICATION INFO.:	US 2003-642122	A1	20030815 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2003-621269, filed on 15 Jul 2003, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-396263P	20020715 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Shelley P.M. Fussey, Williams, Morgan & Amerson, P.C., Suite 1100, 10333 Richmond, Houston, TX, 77042	
NUMBER OF CLAIMS:	26	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	53 Drawing Page(s)	
LINE COUNT:	13330	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 18 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2004:171462 USPATFULL Full-text  
TITLE: Combinations and kits for treating viral infections  
using antibodies to aminophospholipids  
INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES  
Soares, M. Melina, Richardson, TX, UNITED STATES  
Ran, Sophia, Riverton, IL, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004131621	A1	20040708
APPLICATION INFO.:	US 2003-642060	A1	20030815 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2003-621269, filed on 15 Jul 2003, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-396263P	20020715 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Shelley P.M. Fussey, Williams, Morgan & Amerson, P.C., Suite 1100, 10333 Richmond, Houston, TX, 77042	
NUMBER OF CLAIMS:	23	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	53 Drawing Page(s)	
LINE COUNT:	13167	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L9 ANSWER 19 OF 19 USPATFULL on STN

ACCESSION NUMBER: 2004:171451 USPATFULL Full-text  
TITLE: Methods for treating viral infections using antibodies  
to aminophospholipids  
INVENTOR(S): Thorpe, Philip E., Dallas, TX, UNITED STATES  
Soares, M. Melina, Richardson, TX, UNITED STATES  
Ran, Sophia, Riverton, IL, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004131610	A1	20040708
APPLICATION INFO.:	US 2003-642120	A1	20030815 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2003-621269, filed on 15 Jul 2003, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-396263P	20020715 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Shelley P.M. Fussey, Williams, Morgan & Amerson, P.C., Suite 1100, 10333 Richmond, Houston, TX, 77042	
NUMBER OF CLAIMS:	25	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	53 Drawing Page(s)	
LINE COUNT:	13359	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Disclosed are surprising discoveries concerning the role of anionic phospholipids and aminophospholipids in tumor vasculature and in viral entry and spread, and compositions and methods for utilizing these findings in the treatment of cancer and viral infections. Also disclosed are advantageous antibody, immunoconjugate and duramycin-based compositions and combinations that bind and inhibit anionic phospholipids and aminophospholipids, for use in the safe and effective treatment of cancer, viral infections and related diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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(FILE 'HOME' ENTERED AT 09:12:12 ON 08 NOV 2006)

FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 09:12:35 ON 08 NOV 2006

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L2      11744 S "GEMCITABINE"
L3      229 S "VASCULAR TARGETING AGENT?"
L4      16897 S "SOLID TUMOR?"
L5      71 S L1 AND L2
L6      43 S L2 AND L3
L7      38 S L5 AND L4
L8      23 S L1 AND L2 AND L3
L9      19 S L8 AND L4
L10     0 S L5 NOT PY>2001
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L14 170074 "SYNERGISTIC"

=> s l2 and l14

L15 1514 L2 AND L14

=> d his



(FILE 'HOME' ENTERED AT 09:12:12 ON 08 NOV 2006)

FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 09:12:35 ON 08 NOV 2006

L1 538 S "DMXAA" OR "5,6-DIMETHYL-XANTHENE-4 ACETIC ACID"  
L2 11744 S "GEMCITABINE"  
L3 229 S "VASCULAR TARGETING AGENT?"  
L4 16897 S "SOLID TUMOR?"  
L5 71 S L1 AND L2  
L6 43 S L2 AND L3  
L7 38 S L5 AND L4  
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L9 19 S L8 AND L4  
L10 0 S L5 NOT PY>2001  
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L12 0 S L7 NOT PY>2001  
L13 1 S L5 NOT PY>2002  
L14 170074 S "SYNERGISTIC"  
L15 1514 S L2 AND L14

=> s 16 not py>2002

L16 2 L6 NOT PY>2002

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L16 ANSWER 1 OF 2 MEDLINE on STN  
ACCESSION NUMBER: 2002698167 MEDLINE Full-text  
DOCUMENT NUMBER: PubMed ID: 12459376  
TITLE: The development of combretastatin A4 phosphate as a  
vascular targeting agent.  
AUTHOR: Chaplin David J; Hill Sally A  
CORPORATE SOURCE: Oxigene Inc., Watertown, MA 02472, USA..  
dchaplin@oxigene.com  
SOURCE: International journal of radiation oncology, biology,  
physics, (2002 Dec 1) Vol. 54, No. 5, pp. 1491-6.  
Journal code: 7603616. ISSN: 0360-3016.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200301  
ENTRY DATE: Entered STN: 17 Dec 2002  
Last Updated on STN: 3 Jan 2003  
Entered Medline: 2 Jan 2003

AB Purpose: This overview summarizes the preclinical development of tubulin-depolymerizing agents as vascular targeting agents, leading to the identification of combretastatin A4P (CA4P). Methods and Materials: The murine tumor CaNT was implanted s.c. in the dorsum of CBA mice. Vascular function was determined after treatment using the perfusion marker Hoechst 33342 and fluorescence microscopy. Tumor cell response was assessed by using an excision assay and by measuring the delay in growth of treated tumors. Results: At doses that approximated one-half the maximum tolerated dose (MTD) in CBA mice, none of the agents evaluated-i.e., taxol, melphalan, 5-fluorouracil, doxorubicin, cisplatin, gemcitabine, and irinotecan-induced any significant reduction in perfused vascular volume within the tumor mass. In contrast, CA4P at a dose of 100 mg/kg, which approximates one-fifth the MTD, induced a greater than 80% reduction in vascular function. Although colchicine did induce vascular shutdown, this occurred only at doses approximating the MTD. Histologic evaluation demonstrated that continued growth and repopulation of the tumor mass was the result of a surviving rim of viable tumor cells at the

tumor periphery. Conclusion: These results confirm the ability of CA4P to selectively compromise vascular function in experimental tumors, inducing extensive tumor cell death at well-tolerated doses. However, despite these effects, no growth retardation is obtained when CA4P is administered alone in a single dose. The continued growth and repopulation of the tumor mass occurs from a narrow rim of viable cells at the periphery. If, as is believed, these remaining cells are the ones most sensitive to conventional cytotoxic and macromolecular approaches, CA4P and other vascular targeting agents offer considerable potential for enhancing the effectiveness of existing and emerging cancer therapies.

L16 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:896034 CAPLUS Full-text

DOCUMENT NUMBER: 139:316714

TITLE: The development of combretastatin A4 phosphate as a vascular targeting agent

AUTHOR(S): Chaplin, David J.; Hill, Sally A.

CORPORATE SOURCE: Oxigene Inc., Watertown, MA, 02472, USA

SOURCE: International Journal of Radiation Oncology, Biology, Physics (2002), 54(5), 1491-1496  
CODEN: IOBPD3; ISSN: 0360-3016

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Purpose: This overview summarizes the preclin. development of tubulin-depolymg. agents as vascular targeting agents, leading to the identification of combretastatin A4P (CA4P). Methods and Materials: The murine tumor CaNT was implanted s.c. in the dorsum of CBA mice. Vascular function was determined after treatment using the perfusion marker Hoechst 33342 and fluorescence microscopy. Tumor cell response was assessed by using an excision assay and by measuring the delay in growth of treated tumors. Results: At doses that approximated one-half the maximum tolerated dose (MTD) in CBA mice, none of the agents evaluated-i.e., taxol, melphalan, 5-fluorouracil, doxorubicin, cisplatin, gemcitabine, and irinotecan-induced any significant reduction in perfused vascular volume within the tumor mass. In contrast, CA4P at a dose of 100 mg/kg, which approximates one-fifth the MTD, induced a greater than 80% reduction in vascular function. Although colchicine did induce vascular shutdown, this occurred only at doses approximating the MTD. Histol. evaluation demonstrated that continued growth and repopulation of the tumor mass was the result of a surviving rim of viable tumor cells at the tumor periphery. Conclusion: These results confirm the ability of CA4P to selectively compromise vascular function in exptl. tumors, inducing extensive tumor cell death at well-tolerated doses. However, despite these effects, no growth retardation is obtained when CA4P is administered alone in a single dose. The continued growth and repopulation of the tumor mass occurs from a narrow rim of viable cells at the periphery. If, as is believed, these remaining cells are the ones most sensitive to conventional cytotoxic and macromol. approaches, CA4P and other vascular targeting agents offer considerable potential for enhancing the effectiveness of existing and emerging cancer therapies.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 09:12:35 ON 08 NOV

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L2 11744 S "GEMCITABINE"  
L3 229 S "VASCULAR TARGETING AGENT?"  
L4 16897 S "SOLID TUMOR?"  
L5 71 S L1 AND L2  
L6 43 S L2 AND L3  
L7 38 S L5 AND L4  
L8 23 S L1 AND L2 AND L3  
L9 19 S L8 AND L4  
L10 0 S L5 NOT PY>2001  
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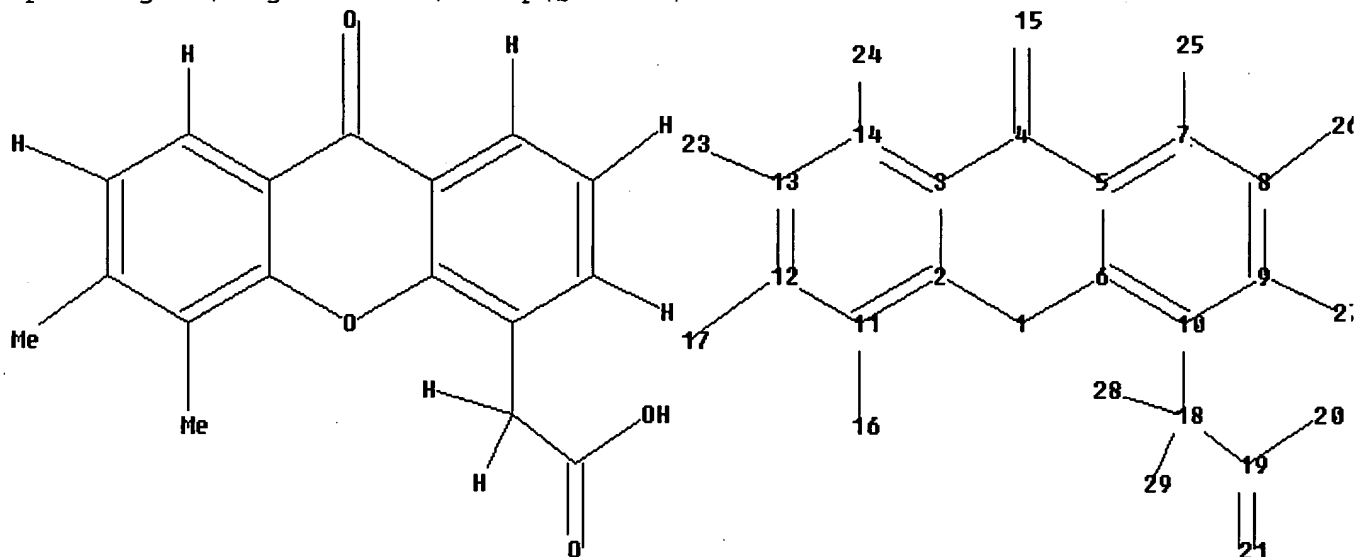
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ring nodes :

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19-21

ring bonds :

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exact/norm bonds :

4-15

exact bonds :

1-2 1-6 3-4 4-5 7-25 8-26 9-27 10-18 11-16 12-17 13-23 14-24 18-19 18-28

18-29

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containing 1 :

Match level :

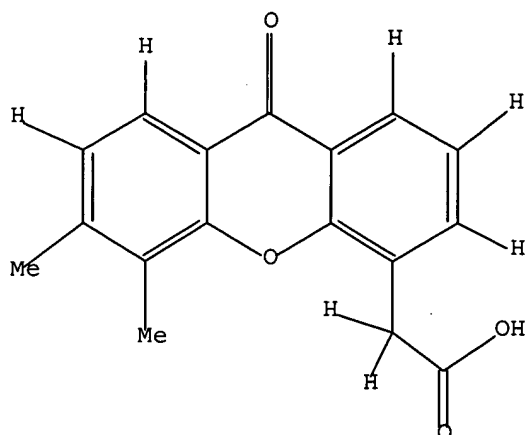
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19:CLASS 20:CLASS 21:CLASS  
23:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS

L1 STRUCTURE UPLOADED

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L1 STR



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BATCH \*\*COMPLETE\*\*

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PROJECTED ANSWERS: 0 TO 0

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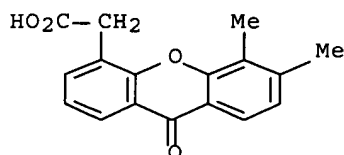
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L3 1 ANSWERS REGISTRY COPYRIGHT 2006 ACS on STN

IN 9H-Xanthene-4-acetic acid, 5,6-dimethyl-9-oxo- (9CI)

MF C17 H14 O4

CI COM



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

ALL ANSWERS HAVE BEEN SCANNED

=> file medline, caplus, wpids, uspatfull

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SEARCH TIME: 00.00.01

0 ITERATIONS

0 ANSWERS

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 0 TO 0

PROJECTED ANSWERS: 0 TO 0

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L5 7 L4 AND "GEMCITABINE"

=> d 15 1-7 ibib, abs, hitstr

L5 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:984120 CAPLUS Full-text

DOCUMENT NUMBER: 143:279360

TITLE: Methods of detecting CD133 antigen (AC133) expression level and use as biomarker for human cancer diagnosis and therapy monitor

INVENTOR(S): Penning, Maarten Tjerk; Van den Broek, Sebastiaan  
Johannes Jacobus; Voest, Emile Eugene; Beerepoot,  
Laurens Victor; Mehra, Niven

PATENT ASSIGNEE(S): Primagen Holding B. V., Neth.; UMC Utrecht Holding B. V.

SOURCE: PCT Int. Appl., 55 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

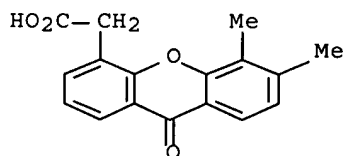
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

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WO 2005083123	A1	20050909	WO 2005-NL155	20050302
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,				

CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,  
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,  
 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,  
 NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM,  
 SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,  
 AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,  
 EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,  
 RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,  
 MR, NE, SN, TD, TG  
 EP 1571225 A1 20050907 EP 2004-75686 20040302  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK  
 CA 2558604 AA 20050909 CA 2005-2558604 20050302  
 PRIORITY APPLN. INFO.: EP 2004-75686 A 20040302  
 US 2004-549450P P 20040302  
 WO 2005-NL155 W 20050302  
 AB This invention provides methods of detecting CD133 antigen (AC133) expression  
 level and use as a biomarker for human cancer diagnosis and therapy monitor.  
 Blood anal. including number of circulating endothelial cells and expression  
 levels of human genes AC133 (CD133), EST032 and U1A evaluated by NASBA anal.,  
 were determined prior to and during chemotherapy using drugs such as  
 angiostatin or PrimMed01, gemcitabine, and cisplatin, for a wide range of  
 human tumor types. A use of a nucleic acid mol. comprising at least part of a  
 sequence of AC133 or an analog thereof for monitoring a treatment of an  
 individual suffering from a disease is also provided, as well as a diagnostic  
 kit comprising such nucleic acid mol.  
 IT 117570-53-3, DMXAA  
 RL: BUU (Biological use, unclassified); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (methods of detecting CD133 antigen (AC133) expression level and use as  
 biomarker for human cancer diagnosis and therapy monitor)  
 RN 117570-53-3 CAPLUS  
 CN 9H-Xanthene-4-acetic acid, 5,6-dimethyl-9-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2005:975665 CAPLUS Full-text  
 DOCUMENT NUMBER: 143:264929  
 TITLE: Methods for detecting AC133 antigen mRNA for diagnosis  
 and treatment of cancer and other diseases  
 INVENTOR(S): Penning, Maarten Tjerk; Beerepoot, Laurens Victor; Van  
 Den Broek, Sebastiaan Johannes Jacobus; Mehra, Niven;  
 Voest, Emile Eugene  
 PATENT ASSIGNEE(S): Primagen Holding B.V., Neth.; UMC Utrecht Holding B.V.  
 SOURCE: Eur. Pat. Appl., 28 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent

LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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CA 2558604	AA	20050909	CA 2005-2558604	20050302
WO 2005083123	A1	20050909	WO 2005-NL155	20050302
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

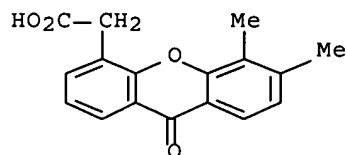
PRIORITY APPLN. INFO.:  
EP 2004-75686 A 20040302  
US 2004-549450P P 20040302  
WO 2005-NL155 W 20050302

AB The invention provides methods for detecting AC133 antigen mRNA for diagnosis and treatment of cancer and other diseases. AC133 antigen mRNA may be quantitated by PCR, RT-PCR, NASBA, SDA, TMA, bDNA or rolling circle amplification. Diseases include cancer and heart disease, high blood pressure, ischemia, stroke, psoriasis, Crohn's disease, rheumatoid arthritis, endometriosis, atherosclerosis, obesity, diabetes mellitus, diabetic retinopathy, macular degeneration, Alzheimer's disease, Peutz Jegher's syndrome, multiple sclerosis, systemic lupus erythematosus, Wegener's granulomatosis, vasculitis, sickle cell disease, thalassemia and angina.

IT 117570-53-3  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(methods for detecting AC133 antigen mRNA for diagnosis and treatment of cancer and other diseases)

RN 117570-53-3 CAPLUS

CN 9H-Xanthene-4-acetic acid, 5,6-dimethyl-9-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 2005:548329 CAPLUS Full-text  
DOCUMENT NUMBER: 143:90113  
TITLE: Emerging drugs for ovarian cancer  
AUTHOR(S): Kelland, Lloyd R.



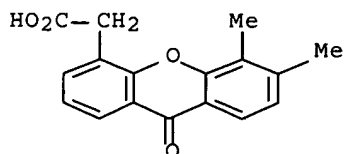
CORPORATE SOURCE: Antisoma Research Laboratories, St Georges Hospital  
Medical School, London, SW17 0QS, UK  
SOURCE: Expert Opinion on Emerging Drugs (2005), 10(2),  
413-424  
CODEN: EOEDA3  
PUBLISHER: Ashley Publications Ltd.  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English

AB A review. Because most patients presenting with advanced ovarian cancer are not curable by surgery alone, chemotherapy represents an essential component of treatment. The disease may be considered as chemosensitive, as in around three-quarters of patients major (complete) responses are seen to initial treatment with the platinum-containing drugs cisplatin and carboplatin either used alone or in combination with the taxane, paclitaxel. However, only 15 - 20% of patients experience long-term remission as tumors often become resistant. The probability of achieving a second response depends on the duration of remission after first-line therapy: if this is < 6 mo (considered as platinum resistant) second responses are uncommon and usually short-lived; if this is > 6, and especially if > 12 mo (platinum sensitive), responses may be seen in about a quarter of patients, to the same drugs as used first line or to drugs such as pegylated liposomal doxorubicin, topotecan and hexamethylmelamine (all three are approved in this setting by the FDA). Gemcitabine, oral etoposide, docetaxel and oxaliplatin also show some activity either in sequential addition to existing approved of first-line therapy (as with gemcitabine) or as second-line therapy. However, there is an urgent unmet clin. need for new drugs capable of prolonging survival either by increasing long-term remission rates and/or duration as first-line treatment or to improve on outcomes of second-line treatment. Strategies currently being exploited in clin. trials include attempts to deliver more killing selectively to tumors (e.g., i.p. administration of cisplatin or radiolabeled monoclonal antibodies), agents designed to target drug resistance mechanisms (e.g., TLK-286 activated by glutathione transferase), agents targeting proteins/receptors shown to be selectively expressed in the disease (e.g., monoclonal antibodies recognizing CA-125 or HER1; small mols. targeting HER1 such as gefitinib) and disrupting established tumor vasculature (e.g., 5,6-di-Me xanthene 4-acetic acid). At the preclin. level, agents being developed to target the phosphatidylinositol 3 kinase/AKT/mTOR pathway, and K-Ras inhibitors, may offer efficacy in the future.

IT 117570-53-3, 5,6-Dimethyl xanthene 4-acetic acid  
RL: PAC (Pharmacological activity); THU. (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(5,6-di-Me xanthene 4-acetic acid disrupting established tumor  
vasculature used in treatment of ovarian cancer in patient)

RN 117570-53-3 CAPLUS

CN 9H-Xanthene-4-acetic acid, 5,6-dimethyl-9-oxo- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

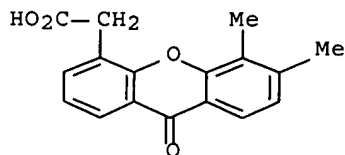
ACCESSION NUMBER: 2003:202462 CAPLUS Full-text  
 DOCUMENT NUMBER: 138:226761  
 TITLE: Synergistic anticancer combinations containing  
 5,6-dimethylxanthenone-4-acetic acid  
 INVENTOR(S): Wilson, William Robert; Siim, Bronwyn Gae  
 PATENT ASSIGNEE(S): Cancer Research Technology Limited, UK  
 SOURCE: PCT Int. Appl., 31 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003020259	A2	20030313	WO 2002-GB4025	20020903
WO 2003020259	A3	20030417		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG CA 2458459 AA 20030313 CA 2002-2458459 20020903 EP 1423105 A2 20040602 EP 2002-758562 20020903 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK BR 2002012258 A 20041019 BR 2002-12258 20020903 JP 2005509599 T2 20050414 JP 2003-524567 20020903 CN 1708296 A 20051214 CN 2002-817257 20020903 NZ 531045 A 20060831 NZ 2002-531045 20020903 NO 2004000591 A 20040430 NO 2004-591 20040210 ZA 2004001078 A 20050415 ZA 2004-1078 20040210 US 2004204480 A1 20041014 US 2004-790943 20040302 PRIORITY APPLN. INFO.: GB 2001-21285 A 20010903 WO 2002-GB4025 W 20020903				

AB The present invention relates to synergistic combinations of the 5,6-dimethylxanthenone-4-acetic acid (DMXAA) and a compound selected from platinum compds., Vinca alkaloids, alkylating agents, anthracyclines, topoisomerase I inhibitors, antimetabolites and topoisomerase II inhibitors, which have antitumor activity. More particularly, the invention is concerned with the use of such combinations in the treatment of cancer and pharmaceutical compds. containing the combinations. The antitumor activity and host toxicity of DMXAA/cytotoxic drug combinations was assessed by varying the dose of chemotherapeutic drug up to the toxicity limit, with co-administration of a fixed DMXAA dose (80  $\mu$ mol/kg, ca. 80% of MTD), and evaluating subsequent tumor growth delay. Of the 7 drugs investigated, 4 (doxorubicin, 5-fluorouracil, cyclophosphamide and cisplatin) had appreciable activity against this tumor as indicated by dose-response relationships providing significant slopes by linear regression, and highly significant growth delays of 10 days at their MTDs.

IT 117570-53-3, 5,6-Dimethylxanthenone-4-acetic acid  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (synergistic anticancer combinations containing dimethylxanthenoneacetic acid)

RN 117570-53-3 CAPLUS  
CN 9H-Xanthene-4-acetic acid, 5,6-dimethyl-9-oxo- (9CI) (CA INDEX NAME)



L5 ANSWER 5 OF 7 USPATFULL on STN

ACCESSION NUMBER: 2005:240102 USPATFULL Full-text  
TITLE: Hydrogels used to deliver medicaments to the eye for  
the treatment of posterior segment diseases  
INVENTOR(S): Schultz, Clyde L., Ponte Vedra, FL, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005208102	A1	20050922
APPLICATION INFO.:	US 2004-821718	A1	20040409 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2003-461354P	20030409 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	FINCH IP LLC, P.O. BOX 1358, CONCORD, NH, 03302, US	
NUMBER OF CLAIMS:	20	
EXEMPLARY CLAIM:	1	
LINE COUNT:	502	

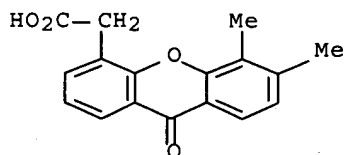
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a polymeric drug delivery system including a hydrogel containing one or more drugs for the treatment of a posterior segment disease. Allowing passive transference of this drug from a dilute solution into the hydrogel produces the delivery system. The hydrogel, when placed in contact with the eye, delivers the drug. The delivery of the drug is sustained over an extended period of time, which is of particular utility in the eye, which is periodically flushed with tears. This sustained delivery accelerates the treatment process while avoiding potential damaging effects of localized delivery of high concentrations of compounds, e.g., from eye drops.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 117570-53-3, DMXAA  
(hydrogels containing drugs for treatment of eye diseases in posterior segment)

RN 117570-53-3 USPATFULL  
CN 9H-Xanthene-4-acetic acid, 5,6-dimethyl-9-oxo- (9CI) (CA INDEX NAME)



L5 ANSWER 6 OF 7 USPATFULL on STN

ACCESSION NUMBER: 2005:87035 USPATFULL Full-text  
 TITLE: Hydrogels used to deliver medicaments to the eye for the treatment of posterior segment diseases  
 INVENTOR(S): Schultz, Clyde L., Ponte Vedra, FL, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005074497	A1	20050407
APPLICATION INFO.:	US 2004-971997	A1	20041022 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2004-821718, filed on 9 Apr 2004, PENDING		

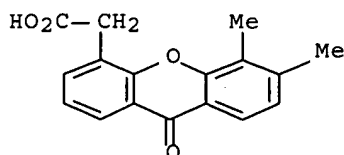
	NUMBER	DATE
PRIORITY INFORMATION:	US 2003-461354P	20030409 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	CLARK & ELBING LLP, 101 FEDERAL STREET, BOSTON, MA, 02110	
NUMBER OF CLAIMS:	27	
EXEMPLARY CLAIM:	1	
LINE COUNT:	582	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB This invention provides a polymeric drug delivery system including a hydrogel containing one or more drugs for the treatment of a posterior segment disease. Exemplary drugs are anti-angiogenesis compounds for the treatment of macular degeneration. Allowing passive transference of this drug from a dilute solution into the hydrogel produces the delivery system. The hydrogel, when placed in contact with the eye, delivers the drug. The delivery of the drug is sustained over an extended period of time, which is of particular utility in the eye, which is periodically flushed with tears. This sustained delivery accelerates the treatment process while avoiding potential damaging effects of localized delivery of high concentrations of compounds, e.g., from eye drops.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 117570-53-3, DMXAA  
 (hydrogels containing drugs for treatment of eye diseases in posterior segment)  
 RN 117570-53-3 USPATFULL  
 CN 9H-Xanthene-4-acetic acid, 5,6-dimethyl-9-oxo- (9CI) (CA INDEX NAME)



L5 ANSWER 7 OF 7 USPATFULL on STN

ACCESSION NUMBER: 2004:261978 USPATFULL Full-text  
 TITLE: Anti-cancer combinations  
 INVENTOR(S): Wilson, William R., Waiuku, NEW ZEALAND  
 Siim, Bronwyn G., Mt. Eden, NEW ZEALAND  
 PATENT ASSIGNEE(S): Cancer Research Technology Limited (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004204480	A1	20041014
APPLICATION INFO.:	US 2004-790943	A1	20040302 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	WO 2002-GB4025	20020903
	GB 2001-21285	20010903
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	PALMER & DODGE, LLP, KATHLEEN M. WILLIAMS; 111 HUNTINGTON AVENUE, BOSTON, MA, 02199	
NUMBER OF CLAIMS:	23	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	2 Drawing Page(s)	
LINE COUNT:	1297	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

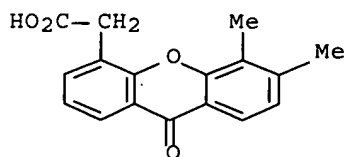
AB The present invention relates to synergistic combinations of the compound 5,6-dimethylxanthenone-4-acetic acid (DMXAA) and a compound selected from platinum compounds, vinca alkaloids, alkylating agents, anthracyclines, topoisomerase I inhibitors, antimetabolites and topoisomerase II inhibitors, which have anti-tumour activity. Preferably, the present invention relates to synergistic combinations of the compound 5,6-dimethylxanthenone-4-acetic acid (DMXAA) and a compound selected from carboplatin, gemcitabine, cisplatin, 5-fluorouracil, cyclophosphamide, etoposide, vincristine, doxorubicin and irinotecan. More particularly, the invention is concerned with the use of such combinations in the treatment of cancer and pharmaceutical compositions containing such combinations. The invention further provides for methods of preparing the combinations of the invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

IT 117570-53-3, 5,6-Dimethylxanthenone-4-acetic acid  
 (synergistic anticancer combinations containing dimethylxanthenoneacetic acid)

RN 117570-53-3 USPATFULL

CN 9H-Xanthene-4-acetic acid, 5,6-dimethyl-9-oxo- (9CI) (CA INDEX NAME)



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(FILE 'HOME' ENTERED AT 09:28:31 ON 08 NOV 2006)

FILE 'REGISTRY' ENTERED AT 09:28:56 ON 08 NOV 2006

L1 STRUCTURE UPLOADED  
L2 0 S L1  
L3 1 S L1 EXA FULL

FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 09:29:39 ON 08 NOV 2006

L4 280 S L3  
L5 7 S L4 AND "GEMCITABINE"

=> s l4 and "combined chemotherapy"

L6 8 L4 AND "COMBINED CHEMOTHERAPY"

=> d l6 1-8 ibib, abs, hitstr

L6 ANSWER 1 OF 8 MEDLINE on STN

ACCESSION NUMBER: 2002733282 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 12497205

TITLE: Marked potentiation of the antitumour activity of  
chemotherapeutic drugs by the antivascular agent  
5,6-dimethylxanthenone-4-acetic acid (DMXAA).

AUTHOR: Siim Bronwyn G; Lee Alan E; Shalal-Zwain Sahar; Pruijn  
Frederik B; McKeage Mark J; Wilson William R

CORPORATE SOURCE: Molecular Medicine and Pathology, The University of  
Auckland, Private Bag 92019, Auckland, New Zealand.

SOURCE: Cancer chemotherapy and pharmacology, (2003 Jan) Vol. 51,  
No. 1, pp. 43-52. Electronic Publication: 2002-11-12.  
Journal code: 7806519. ISSN: 0344-5704.

PUB. COUNTRY: Germany: Germany, Federal Republic of

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200302

ENTRY DATE: Entered STN: 27 Dec 2002

Last Updated on STN: 26 Feb 2003

Entered Medline: 25 Feb. 2003

AB PURPOSE. To determine whether there is a therapeutic interaction between the  
antivascular agent 5,6-dimethylxanthenone-4-acetic acid (DMXAA) and nine  
chemotherapy drugs against an early-passage mouse mammary tumour (MDAH-MCa-4),  
and to investigate the mechanism of any such interaction. METHODS AND RESULTS.  
Female C3H/HeN mice bearing intramuscular MDAH-MCa-4 tumours were injected  
intraperitoneally with DMXAA (80 micro mol/kg) or chemotherapy drug (at a  
range up to the maximum tolerated dose) alone, or coadministered. A small  
reduction in the dose of the chemotherapy drug was required in most cases, but  
the increase in antitumour effect was much greater than the increase in host  
toxicity (body weight loss). The therapeutic gain increased in the order 5-  
fluorouracil (no gain)<(etoposide, carboplatin, cyclophosphamide, doxorubicin,

cisplatin)<(docetaxel, vincristine)<paclitaxel. The interaction with paclitaxel (31.6 micro mol/kg) was striking, with coadministration of DMXAA extending the median tumour growth delay from 0.3 to 80 days with three of seven animals cured. The interaction showed a broad timing of the optimum with similar activity when paclitaxel was administered 4 h before to 1 h after DMXAA. No therapeutic synergy was obtained when paclitaxel was combined with the antivasular agent combretastatin A4 phosphate (227 micro mol/kg), which induced only transient blood flow inhibition in this tumour, measured using the H33342 perfusion marker. Paclitaxel did not enhance the antivasular activity of DMXAA. Plasma and tumour concentrations of paclitaxel (and carboplatin), measured by LC-MS and ICP-MS respectively, were not elevated by combination with DMXAA. CONCLUSIONS. There was a dramatic therapeutic interaction between DMXAA and standard chemotherapy drugs, particularly paclitaxel, against the MDAH-MCa-4 tumour, which was not due to a pharmacokinetic interaction or potentiation of antivasular activity. It is suggested that the major mechanism of synergy is killing of cells by DMXAA in poorly perfused regions of tumours that are inaccessible to chemotherapy drugs.

L6 ANSWER 2 OF 8 MEDLINE on STN  
 ACCESSION NUMBER: 2002625620 MEDLINE Full-text  
 DOCUMENT NUMBER: PubMed ID: 12382527  
 TITLE: Potential of DMXAA combination therapy for solid tumors.  
 AUTHOR: Baguley Bruce C; Wilson William R  
 CORPORATE SOURCE: Auckland Cancer Society Research Centre, University of  
 Auckland, Auckland, New Zealand.. b.baguley@auckland.ac.nz  
 SOURCE: Expert review of anticancer therapy, (2002 Oct) Vol. 2, No.  
 5, pp. 593-603. Ref: 84  
 Journal code: 101123358. ISSN: 1473-7140.  
 PUB. COUNTRY: England: United Kingdom  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 General Review; (REVIEW)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200308  
 ENTRY DATE: Entered STN: 18 Oct 2002  
 Last Updated on STN: 28 Aug 2003  
 Entered Medline: 27 Aug 2003

AB DMXAA is one of the first examples of a new class of anticancer agents that attack existing tumor blood vessels and thus deprives tumor tissue of an adequate blood supply. Its mechanism of action appears to rely on the induction within tumor tissue of cytokines, such as tumor necrosis factor. In experimental tumors, DMXAA interacts productively with radiation, hyperthermia and a number of chemotherapeutic drugs. This review discusses the mechanisms underlying such interactions and how these might be exploited in clinical cancer treatment.

L6 ANSWER 3 OF 8 MEDLINE on STN  
 ACCESSION NUMBER: 2002211409 MEDLINE Full-text  
 DOCUMENT NUMBER: PubMed ID: 11948484  
 TITLE: Vascular targeting agents enhance chemotherapeutic agent  
 activities in solid tumor therapy.  
 AUTHOR: Siemann Dietmar W; Mercer Emma; Lepler Sharon; Rojiani Aryn  
 M  
 CORPORATE SOURCE: Department of Radiation Oncology, Shands Cancer Center,  
 University of Florida, Gainesville, FL 32610, USA..  
 siemadw@ufl.edu  
 CONTRACT NUMBER: CA84408 (NCI)

SOURCE: International journal of cancer. Journal international du cancer, (2002 May 1) Vol. 99, No. 1, pp. 1-6.  
Journal code: 0042124. ISSN: 0020-7136.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200205  
ENTRY DATE: Entered STN: 12 Apr 2002  
Last Updated on STN: 2 May 2002  
Entered Medline: 1 May 2002

AB The utility of combining the vascular targeting agents 5,6-dimethyl-xanthenone-4 acetic acid (DMXAA) and combretastatin A-4 disodium phosphate (CA4DP) with the anticancer drugs cisplatin and cyclophosphamide (CP) was evaluated in experimental rodent (KHT sarcoma), human breast (SKBR3) and ovarian (OW-1) tumor models. Doses of the vascular targeting agents that led to rapid vascular shutdown and subsequent extensive central tumor necrosis were identified. Histologic evaluation showed morphologic damage of tumor cells within a few hours after treatment, followed by extensive hemorrhagic necrosis and dose-dependent neoplastic cell death as a result of prolonged ischemia. Whereas these effects were induced by a range of CA4DP doses (10-150 mg/kg), the dose response to DMXAA was extremely steep; doses  $\leq$  15 mg/kg were ineffective and doses  $\geq$  20 mg/kg were toxic. DMXAA also enhanced the tumor cell killing of cisplatin, but doses  $>$  15 mg/kg were required. In contrast, CA4DP increased cisplatin-induced tumor cell killing at all doses studied. This enhancement of cisplatin efficacy was dependent on the sequence and interval between the agents. The greatest effects were achieved when the vascular targeting agents were administered 1-3 hr after cisplatin. When CA4DP (100 mg/kg) or DMXAA (17.5 mg/kg) were administered 1 hr after a range of doses of cisplatin or CP, the tumor cell kill was 10-500-fold greater than that seen with chemotherapy alone. In addition, the inclusion of the antivascular agents did not increase bone marrow stem cell toxicity associated with these anticancer drugs, thus giving rise to a therapeutic gain. Copyright 2002 Wiley-Liss, Inc.

L6 ANSWER 4 OF 8 MEDLINE on STN  
ACCESSION NUMBER: 2002135262 MEDLINE Full-text  
DOCUMENT NUMBER: PubMed ID: 11870905  
TITLE: Differential sensitivity of two adenocarcinoma xenografts to the anti-vascular drugs combretastatin A4 phosphate and 5,6-dimethylxanthenone-4-acetic acid, assessed using MRI and MRS.  
AUTHOR: Beauregard Daniel A; Pedley R Barbara; Hill Sally A; Brindle Kevin M  
CORPORATE SOURCE: Department of Biochemistry, University of Cambridge, Cambridge CB2 1GA, UK.  
SOURCE: NMR in biomedicine, (2002 Apr) Vol. 15, No. 2, pp. 99-105.  
Journal code: 8915233. ISSN: 0952-3480.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200206  
ENTRY DATE: Entered STN: 1 Mar 2002  
Last Updated on STN: 21 Jun 2002  
Entered Medline: 20 Jun 2002

AB The effects of two anti-vascular agents, combretastatin A4 phosphate (CA4P), and 5,6-dimethylxanthenone-4-acetic acid (DMXAA), on the perfusion of two human colon adenocarcinomas implanted in SCID mice, were assessed for up to 3



h using non-invasive magnetic resonance imaging (MRI) and spectroscopy techniques (MRS). MRI measurements of GdDTPA inflow showed that treatment with CA4P had little effect on the perfusion of HT29 tumours. Localized (31)P MRS measurements also showed that the drug had no significant effect on tumour cell energy status, as assessed from the ratio of the integrals of the signals from inorganic phosphate (P(i)) and nucleoside triphosphates. However, after treatment with DMXAA, perfusion was reduced and the P(i)/NTP ratio increased, indicating that the HT29 tumour is susceptible to the action of this drug. The LS174T tumour model was susceptible to both CA4P and DMXAA, using the criteria of changes in GdDTPA inflow and P(i)/NTP ratio.

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L6 ANSWER 5 OF 8 MEDLINE on STN

ACCESSION NUMBER: 2002133988 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 11868972

TITLE: Species differences in the metabolism of the antitumour agent 5,6-dimethylxanthene-4-acetic acid in vitro: implications for prediction of metabolic interactions in vivo.

AUTHOR: Zhou S F; Tingle M D; Kestell P; Paxton J W

CORPORATE SOURCE: Division of Pharmacology and Clinical Pharmacology, Faculty of Medical and Health Sciences, University of Auckland, New Zealand.. shufeng.zhou@auckland.ac.nz

SOURCE: Xenobiotica; the fate of foreign compounds in biological systems, (2002 Feb) Vol. 32, No. 2, pp. 87-107. Journal code: 1306665. ISSN: 0049-8254.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200209

ENTRY DATE: Entered STN: 1 Mar 2002

Last Updated on STN: 6 Sep 2002

Entered Medline: 4 Sep 2002

AB 1. Mouse studies have indicated that the antitumour effects of 5,6-dimethylxanthene-4-acetic acid (DMXAA) are dramatically potentiated in combination with other drugs, and it has been proposed that optimization of the therapeutic potential of DMXAA would exploit combination therapy. The aim was to identify the most appropriate animal model for further investigations of the pharmacokinetics of possible DMXAA-drug combinations and their extrapolation to patients. 2. Qualitatively, the metabolic profile for DMXAA in liver microsomes was similar in mouse, rat, rabbit and humans, with glucuronidation and 6-methylhydroxylation the two major metabolic pathways. In all species, the intrinsic clearance by glucuronidation was at least 2-fold that due to hydroxylation. There was significant variability in the in vitro kinetic parameters (Km, Vmax), with the mouse being the least efficient DMXAA metabolizer compared with the other species. 3. Mouse, rat and rabbit renal microsomes exhibited DMXAA glucuronidation activity, but only the rabbit showed 6-methylhydroxylation. For the total in vitro CL(int) (Vmax/Km) by glucuronidation and 6-methylhydroxylation, the ratio of kidney:liver was 0.67, 0.03 and 0.34 in the mouse, rat and rabbit respectively. However, taking into account the liver and kidney weight difference, it is apparent that the in vivo renal metabolism would not be a major contributor to the overall elimination of DMXAA. 4. The inhibitory profile for liver DMXAA glucuronidation was similar across species, but there was remarkable interspecies variability in the inhibition of liver DMXAA 6methylhydroxylation. 5. Extrapolation of in vitro intrinsic clearance to in vivo gave a significant underestimation of plasma clearance for all species. However, there was a significant allometric relationship for plasma clearance

and volume of distribution, but not for maximum tolerated dose across species. 6. The results indicate that animal models may have a limited role in the extrapolation to patients of drug interactions with agents such as DMXAA that have immunomodulating activity that may vary widely between species.

L6 ANSWER 6 OF 8 MEDLINE on STN  
ACCESSION NUMBER: 2001189654 MEDLINE Full-text  
DOCUMENT NUMBER: PubMed ID: 11280751  
TITLE: Vascular attack by 5,6-dimethylxanthenone-4-acetic acid combined with B7.1 (CD80)-mediated immunotherapy overcomes immune resistance and leads to the eradication of large tumors and multiple tumor foci.  
AUTHOR: Kanwar J R; Kanwar R K; Pandey S; Ching L M; Krissansen G W  
CORPORATE SOURCE: Department of Molecular Medicine, School of Medicine and Health Science, University of Auckland, New Zealand.  
SOURCE: Cancer research, (2001 Mar 1) Vol. 61, No. 5, pp. 1948-56. Journal code: 2984705R. ISSN: 0008-5472.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200104  
ENTRY DATE: Entered STN: 25 Apr 2001  
Last Updated on STN: 25 Apr 2001  
Entered Medline: 19 Apr 2001

AB The promise of cancer immunotherapy is that it will not only eradicate primary tumors but will generate systemic antitumor immunity capable of destroying distant metastases. A major problem that must first be surmounted relates to the immune resistance of large tumors. Here we reveal that immune resistance can be overcome by combining immunotherapy with a concerted attack on the tumor vasculature. The functionally related antitumor drugs 5,6-dimethylxanthenone-4-acetic acid (DMXAA) and flavone acetic acid (FAA), which cause tumor vasculature collapse and tumor necrosis, were used to attack the tumor vasculature, whereas the T-cell costimulator B7.1 (CD80), which costimulates T-cell proliferation via the CD28 pathway, was used to stimulate antitumor immunity. The injection of cDNA (60-180 microg) encoding B7.1 into large EL-4 tumors (0.8 cm in diameter) established in C57BL/6 mice, followed 24 h later by i.p. administration of either DMXAA (25 mg/kg) or FAA (300 mg/kg), resulted in complete tumor eradication within 2-6 weeks. In contrast, monotherapies were ineffective. Both vascular attack and B7.1 immunotherapy led to up-regulation of heat shock protein 70 on stressed and dying tumor cells, potentially augmenting immunotherapy. Remarkably, large tumors took on the appearance of a wound that rapidly ameliorated, leaving perfectly healed skin. Combined therapy was mediated by CD8+ T cells and natural killer cells, accompanied by heightened and prolonged antitumor cytolytic activity ( $P < 0.001$ ), and by a marked increase in tumor cell apoptosis. Cured animals completely rejected a challenge of  $1 \times 10^7$  parental EL-4 tumor cells but not a challenge of  $1 \times 10^4$  Lewis lung carcinoma cells, demonstrating that antitumor immunity was tumor specific. Adoptive transfer of  $2 \times 10^8$  splenocytes from treated mice into recipients bearing established (0.8 cm in diameter) tumors resulted in rapid and complete tumor rejection within 3 weeks. Although DMXAA and B7.1 monotherapies are complicated by a narrow range of effective doses, combined therapy was less dosage dependent. Thus, a broad range of amounts of B7.1 cDNA were effective in combination with 25 mg/kg DMXAA. In contrast, DMXAA, which has a very narrow range of high active doses, was effective at a low dose (18 mg/kg) when administered with a large amount (180 microg) of B7.1 cDNA. Importantly, combinational therapy generated heightened antitumor immunity, such that gene transfer of B7.1 into one tumor, followed by systemic DMXAA treatment, led to the complete rejection

of multiple untreated tumor nodules established in the opposing flank. These findings have important implications for the future direction and utility of cancer immunotherapies aimed at harnessing patients' immune responses to their own tumors.

L6 ANSWER 7 OF 8 MEDLINE on STN  
ACCESSION NUMBER: 1999287394 MEDLINE Full-text  
DOCUMENT NUMBER: PubMed ID: 10360649  
TITLE: Thalidomide increases both intra-tumoural tumour necrosis factor-alpha production and anti-tumour activity in response to 5,6-dimethylxanthenone-4-acetic acid.  
AUTHOR: Cao Z; Joseph W R; Browne W L; Mountjoy K G; Palmer B D; Baguley B C; Ching L M  
CORPORATE SOURCE: Auckland Cancer Society Research Centre, University of Auckland School of Medicine, New Zealand.  
SOURCE: British journal of cancer, (1999 May) Vol. 80, No. 5-6, pp. 716-23.  
Journal code: 0370635. ISSN: 0007-0920.  
PUB. COUNTRY: SCOTLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals; AIDS  
ENTRY MONTH: 199906  
ENTRY DATE: Entered STN: 12 Jul 1999  
Last Updated on STN: 12 Jul 1999  
Entered Medline: 23 Jun 1999

AB 5,6-Dimethylxanthenone-4-acetic acid (DMXAA), synthesized in this laboratory and currently in phase I clinical trial, is a low molecular weight inducer of tumour necrosis factor-alpha (TNF-alpha). Administration of DMXAA to mice with established transplantable tumours elicits rapid vascular collapse selectively in the tumour, followed by extensive haemorrhagic necrosis mediated primarily through the production of TNF-alpha. In this report we have investigated the synthesis of TNF-alpha mRNA in hepatic, splenic and tumour tissue. Co-administration of thalidomide with DMXAA increased anti-tumour activity and increased intra-tumoural TNF-alpha production approximately tenfold over that obtained with DMXAA alone. Thalidomide increased splenic TNF-alpha production slightly but significantly decreased serum and hepatic levels of TNF-alpha induced with DMXAA. Lipopolysaccharide (LPS) induced 300-fold higher serum TNF-alpha than did DMXAA at the maximum tolerated dose, but induced similar amounts of TNF-alpha in spleen, liver and tumour. Splenic TNF-alpha activity induced with LPS was slightly increased with thalidomide, but serum and liver TNF-alpha levels were suppressed. Thalidomide did not increase intra-tumoural TNF-alpha production induced with LPS, in sharp contrast to that obtained with DMXAA. While thalidomide improved the anti-tumour response to DMXAA, it had no effect on the anti-tumour action of LPS that did not induce a significant growth delay or cures against the Colon 38 tumour. The increase in the anti-tumour action by thalidomide in combination with DMXAA corresponded to an increase in intra-tumoural TNF-alpha production. Co-administration of thalidomide may represent a novel approach to improving selective intra-tumoural TNF-alpha production and anti-tumour efficacy of DMXAA.

L6 ANSWER 8 OF 8 MEDLINE on STN  
ACCESSION NUMBER: 1998379881 MEDLINE Full-text  
DOCUMENT NUMBER: PubMed ID: 9716024  
TITLE: Enhancement of the anti-tumour effects of the antivasculature agent 5,6-dimethylxanthenone-4-acetic acid (DMXAA) by combination with 5-hydroxytryptamine and bioreductive drugs.

AUTHOR: Lash C J; Li A E; Rutland M; Baguley B C; Zwi L J; Wilson W  
R  
CORPORATE SOURCE: Department of Pathology, The University of Auckland, New  
Zealand.  
CONTRACT NUMBER: N01-CM-47019 (NCI)  
SOURCE: British journal of cancer, (1998 Aug) Vol. 78, No. 4, pp.  
439-45.  
Journal code: 0370635. ISSN: 0007-0920.  
PUB. COUNTRY: SCOTLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199809  
ENTRY DATE: Entered STN: 17 Sep 1998  
Last Updated on STN: 17 Sep 1998  
Entered Medline: 4 Sep 1998

AB The tumour blood flow inhibitor 5,6-dimethylxanthenone-4-acetic acid (DMXAA) causes dramatic haemorrhagic necrosis in murine tumours, but activity is seen only at doses close to the toxic limit. This study investigates two approaches for increasing the therapeutic ratio of DMXAA. The first approach combines DMXAA with a second tumour blood flow inhibitor, 5-hydroxytryptamine (5-HT). Co-administration of 5-HT (700 micromol kg<sup>-1</sup>) to C3H mice caused marked enhancement of DMXAA effects against MDAH-MCa-4 tumours, with dose-modifying factors (DMFs) of >3 for blood flow inhibition (at 4 h), 2.3 for necrosis (at 12 h) and 2.0 for growth delay, without compromising the maximum tolerated dose of DMXAA (90 micromol kg<sup>-1</sup>). The data are consistent with ischaemic injury to the tumour being the major mechanism of anti-tumour activity. The second approach combines DMXAA (+/- 5-HT) with hypoxia-selective bio-reductive drugs. Anti-tumour activity of all three bio-reductive drugs tested (tirapazamine, CI-1010, SN 23816) was strongly potentiated by DMXAA, suggesting that there is a population of reversibly hypoxic tumour cells after DMXAA treatment. Co-administration of 5-HT further potentiated anti-tumour activity, but also increased host toxicity of tirapazamine and CI-1010 so that little therapeutic benefit was achieved. In contrast, the host toxicity of the dinitrobenzamide mustard SN 23816 was only slightly increased by DMXAA/5-HT, whereas the tumour growth delay at the maximum tolerated dose of SN 23816 was increased from 3.5 to 26.5 days. This study demonstrates that 5-HT and/or bio-reductive drugs can improve the therapeutic activity of DMXAA in mice, and that with SN 23816 both approaches can be used together to provide considerably enhanced anti-tumour activity.

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(FILE 'HOME' ENTERED AT 09:28:31 ON 08 NOV 2006)

FILE 'REGISTRY' ENTERED AT 09:28:56 ON 08 NOV 2006

L1 STRUCTURE UPLOADED  
L2 0 S L1  
L3 1 S L1 EXA FULL

FILE 'MEDLINE, CAPLUS, WPIDS, USPATFULL' ENTERED AT 09:29:39 ON 08 NOV  
2006

L4 280 S L3  
L5 7 S L4 AND "GEMCITABINE"  
L6 8 S L4 AND "COMBINED CHEMOTHERAPY"

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